SURGERY FOR CONGENITAL HEART DISEASE

ONE-STAGE COMPLETE UNIFOCALIZATION IN INFANTS: WHEN SHOULD THE VENTRICULAR SEPTAL DEFECT BE CLOSED?

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Background: **The decision whether to close the ventricular septal defect at the time of unifocalization in patients with pulmonary atresia, ventricular septal defect, and major aortopulmonary collaterals may be difficult. The purpose of this study was to develop morphologic and physiologic methods to aid in deciding whether to close the ventricular septal defect in patients undergoing one-stage unifocalization.** ***Methods:*** **Between July 1992 and April 1996, 27 infants with pulmonary atresia, ventricular septal defect, and aortopulmonary collaterals were treated at our institution. Midline complete unifocalization was performed in 25 patients—the ventricular septal defect was closed in 17 and left open in eight. Two patients with severe distal collateral stenoses underwent staged unifocalization. Pulmonary artery and collateral sizes were measured from preoperative angiograms and used to calculate the indexed cross-sectional area of the total neopulmonary artery bed. An intraoperative pulmonary flow study previously validated with experiments in neonatal lambs was performed in six patients: the unifocalized neopulmonary arteries were perfused with a known flow and pulmonary artery pressures were recorded.** ***Results:*** **The neopulmonary artery index was greater in patients who underwent ventricular septal defect closure than in those who did not ($p = 0.001$), although the values did overlap. This index correlated with the postoperative right ventricular/left ventricular pressure ratio ($p = 0.037$). Mean pulmonary artery pressures obtained during the intraoperative flow study and after bypass were comparable.** ***Conclusion:*** **The total neopulmonary artery index correlates with postrepair right ventricular/left ventricular pressure ratio and is useful in deciding when to close the ventricular septal defect if it is larger than 200 mm^2/m^2. The pulmonary flow study is helpful in deciding whether to close the ventricular septal defect in all patients. (J Thorac Cardiovasc Surg 1997;113:858-68)**

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Pulmonary atresia with ventricular septal defect (VSD) and major aortopulmonary collateral arteries (MAPCAs) is a complex lesion with consistent intracardiac abnormalities but with marked heterogeneity of the pulmonary vascular supply.[1-3] The ultimate goal of surgical management of these patients is to achieve a completely separated, in-series, two-ventricle circulation. The conventional approach is staged unifocalization of the MAPCAs and pulmonary arteries (if present), followed by VSD closure.[4-9] This often involves multiple operations before complete repair is achieved. However, a substantial number of patients cannot undergo cor-

rection with this approach. We have adopted a strategy of complete unifocalization in a single stage.[10] Complete repair, including VSD closure and placement of a right ventricle–pulmonary artery conduit, is often achieved during the same operation. In our experience, the majority of the patients (about 95%) can undergo complete unifocalization in one stage from the midline approach. The question of whether to close the VSD at the time of complete unifocalization is a difficult and critical one, and proper criteria have yet to be established. The criteria established for predicting the postrepair right ventricular pressure and right ventricular/left ventricular pressure ratio (pRV/pLV)[11] in cases of traditional tetralogy of Fallot cannot be applied in this lesion, because of the severe arborization defects of the pulmonary blood supply, multiple sources of pulmonary blood flow, and frequently diminutive or absent true pulmonary arteries. The method of measuring the central pulmonary arteries and calculating their cross-sectional areas[12] is not useful after unifocalization because the central pulmonary arteries have generally been augmented surgically. In staged repairs, the decision to complete the repair can be assessed by calculating the pulmonary/systemic blood flow ratio at a second catheterization if the pulmonary blood supply is centralized to one source after unifocalization, provided that no resistance elements are present proximal to the vascular bed, such as a restrictive shunt or a significant pulmonary artery stenosis. However, in the one-stage approach to complete repair this is not an option. It is critical that the decision to close the VSD be correct. Closing the VSD when it should have been left open portends a bad outcome because of the resulting high right ventricular pressures. On the other hand, leaving the VSD open when it should have been closed will result in pulmonary overcirculation and its attendant negative consequences. We have recently developed methods for determining whether VSD closure is suitable during one-stage unifocalization, and we report herein on these methods and their results.

Patients and methods

Between July 1992 and April 1996, 41 patients aged 0.3 months to 37 years who had pulmonary atresia with VSD and MAPCAs were surgically treated at our institution. Techniques of surgical repair have been previously published.[10] Twenty-seven of these patients (66%) were infants whose ages ranged from 10 days to 11.8 months (median 4 months), five of whom were included in our original report of the single-stage repair technique.[10] The remaining 14 older patients underwent correction at the time of initial referral. Of the 27 infants, 17 (group I) underwent complete one-stage repair, including unifocalization, VSD closure, and a right ventricle–pulmonary artery conduit. Eight infants (group II) underwent complete unifocalization in one stage but without VSD closure. The neopulmonary arteries were connected to a shunt in four patients, to the right ventricle by an allograft conduit in three patients, and by transannular patch pulmonary outflow tract reconstruction in one patient. Two patients (group III) underwent staged unifocalization. Of the patients who underwent full repair in a single stage (group I), one had to have the VSD reopened. One group II patient required VSD closure during the same hospitalization because of excessive pulmonary blood flow. Multiorgan failure in association with excessive pulmonary blood flow developed in a second group II patient, who underwent banding of the right ventricle–pulmonary artery conduit.

Attempts to develop criteria for VSD closure

Morphologic data. We hypothesized that objective preoperative assessment of the cumulative cross-sectional area of all collateral vessels and the true pulmonary arteries might be helpful in determining whether VSD closure should be performed. We also hypothesized that collateral stenoses that were surgically accessible during unifocalization (in our experience, stenoses extending out to but not including segmental level vessels) would be of no consequence, but that stenoses at the segmental vessel level or beyond (surgically inaccessible in most cases) would be important in deciding whether to close the VSD. We did not consider classic microvascular pulmonary vascular obstructive disease to be an important issue inasmuch as these procedures are routinely performed in young infants.

Method of measuring MAPCA and pulmonary artery sizes. A retrospective review of the angiograms of all infants was done to measure the sizes of the MAPCAs and true pulmonary arteries when present. In addition, the number of segments effectively supplied by the MAPCAs or the true pulmonary arteries was assessed, and the number of segmental level stenoses in the MAPCAs was recorded. Stenosis in the MAPCAs at the lobar level was not taken into account, because the anastomosis was invariably performed beyond that site of stenosis. The true pulmonary arteries were measured just before their bifurcation, as described by Nakata and associates.[12] MAPCA diameters were measured distal to the surgical unifocalization point. If the segmental level branches were unifocalized separately, they were considered independent vessels and the diameters of these vessels were measured distal to the site of unifocalization. The site of surgical unifocalization was determined from intraoperative observation and the surgical operation records.

All measurements were made by a reviewer who was blinded to the clinical and operative details of the patients, including whether the VSD had been closed. Measurements were made twice and the average of the two values was recorded for analysis. Measurements were corrected for magnification by relating measured diameters to the measured catheter diameter, then calibrating

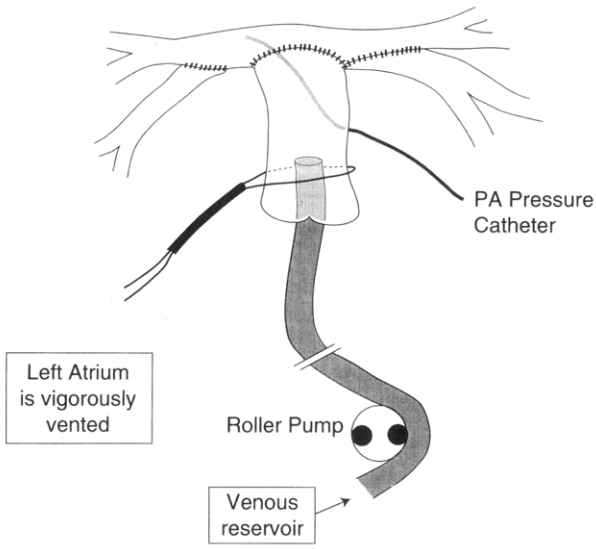

Fig. 1. Schematic representation of the flow study. A separate pump head is used to pump blood from the venous reservoir through a cannula placed in the allograft conduit. A pulmonary artery *(PA)* pressure catheter is used to determine mean pulmonary artery pressure while the left atrium is vigorously vented.

the ratio according to the known catheter size. Indices were determined by calculating cross-sectional area (square millimeter; with the assumption of circular cross-sectional area at the points measured) and dividing this by body surface area (square meter), giving units of square millimeters per square meter. The sum of the total MAPCA index and the pulmonary artery index was called the total neopulmonary arterial index (TNPAI). Segmental level stenoses were considered significant if the luminal diameter was narrowed by more than 25%. The number of segmental stenoses present in each patient was noted. In patients who underwent VSD closure (group I), intraoperative postrepair right and left ventricular pressures were recorded simultaneously. The left ventricular systolic pressure was obtained by measuring the central aortic pressure, and the right ventricular systolic pressure was measured directly by placing a pressure catheter.

Physiologic data. We also hypothesized that preoperative morphologic data, although helpful, would be of only limited use in deciding about VSD closure, because the precision of the technical exercise of complete unifocalization is likely to have an important influence on the eventual total pulmonary vascular cross-sectional area that is achieved after complete unifocalization. Therefore we determined that an immediate assessment of the success of the unifocalization during cardiopulmonary bypass would provide important information.

Intraoperative pulmonary flow study. An intraoperative physiologic study was performed in six recent patients to predict successful closure of the VSD. In these patients, after complete unifocalization and distal conduit anastomosis, while the patient was still supported by bypass, a pulmonary artery catheter and a perfusion cannula were placed through the allograft conduit, and the left atrium was vented (Fig. 1). Incremental volumes of blood (milliliters per minute; equal to 0.25, 0.5, 0.75, 1.0, 1.25, and 1.5 times the predicted early postoperative cardiac index of 2.5 L/min per square meter) were pumped (nonpulsatile flow) through the unifocalized pulmonary arteries with the use of a standard roller pump; by contrast, pulmonary artery and left atrial pressures were recorded at each steady state flow rate. In our first two patients, the data were obtained but no decision was made on the basis of these data. In the third patient, who had previously undergone complete unifocalization with VSD closure and was being reoperated on for pulmonary arterioplasty, the study was performed and the postbypass pulmonary artery pressures were recorded, not for the purpose of decision-making but for assessment of the study method. In the last three of these patients, we used the flow study data prospectively to decide during the operation whether to close the VSD.

Experimental pulmonary flow study. In four normal neonatal lambs (aged 3 to 4 weeks), the pulmonary flow study was conducted. The lambs were premedicated with ketamine, intubated, and their lungs were ventilated with 100% oxygen with a Healthdyne pediatric time-cycled, pressure-limited ventilator (Healthdyne Inc., Marietta, Ga.). A jugular venous line and a femoral arterial line were placed. Anesthesia was maintained by halothane (1% to 2%). After median sternotomy, the pericardium was opened, and left atrial and pulmonary arterial (into the left pulmonary artery) pressure monitoring catheters were placed. An ultrasonic flow probe (Transonic Systems Inc., Ithaca, N.Y.) was placed around the main pulmonary artery to measure the pulmonary blood flow. Baseline pulmonary arterial pressure, left atrial pressure, aortic pressure, and pulmonary blood flow were recorded. Cardiopulmonary bypass was then instituted with the use of standard neonatal techniques and the lambs were cooled to 25° C. After 1 hour of bypass at this temperature, cardioplegic solution was given and the left atrium was vented. The main pulmonary artery was perfused with a roller pump with flows (monitored with an in-line ultrasonic flow probe) equal to 0.25, 0.50, 0.75, 1.0, and 1.5 times the prebypass pulmonary blood flow, while the lungs were ventilated. Pulmonary arterial and left atrial pressures were recorded at each flow rate. The lambs were then rewarmed and bypass was discontinued by means of standard neonatal bypass techniques. The baseline measurements were recorded again. After completion of the study, the lambs were put to death with an overdose of pentobarbital. All animals received humane care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources and published by the National Institutes of Health (NIH Publication No. 86-23, revised 1985). The experimental protocol was approved by the Committee for Animal Care at the University of California, San Francisco.

Data analysis. Descriptive statistics are presented as median and range or 95% confidence intervals (CI). In

Table I. *Patient demographics*

	One-stage unifocalization		*Staged unifocalization*
	VSD closed (group I)	*VSD open (group II)*	*VSD open (group III)*
No. of patients	17	8	2
Age (mo)			
Median	3.6	4.4	3.0 and 8.6
Range	0.3-10.2	1.6-11.8	
Weight (kg)			
Median	3.8	5.4	3.2 and 5.8
Range	2.4-8.3	4.2-7.7	

VSD, Ventricular septal defect.

Table II. *Characteristics of MAPCAs and true PAs*

	One-stage focalization		*Staged unifocalization*
	VSD closed (group I)	*VSD open (group II)*	*VSD open (group III)*
MAPCAs			
No. of MAPCAs per patient			
Median	4	3	4 and 6
Range	1-5	2-6	
Lung segments supplied			
Median	15.0	17.5	20 and 20
Range	4-20	0-20	
Segmental level stenoses			
Median	0	2.5	4 and 8
Range	0-7	0-8	
True PAs			
PAs present	12	5	0
PAs absent	5	3	2
Lung segments supplied by PAs			
Median	5.0	2.5	0 and 0
Range	0-20	0-16	

MAPCA, Major aortopulmoary collateral artery; *PA,* pulmonary artery; *VSD,* ventricular septal defect.

group I, correlation between the calculated TNPAI and the postrepair pRV/pLV ratio was assessed by linear regression analysis. The unpaired *t* test was used to compare the number of MAPCAs, the number of segments supplied by MAPCAs, and the number of segmental stenoses between patients who did and did not undergo VSD closure. The Mann-Whitney test was used to compare the TNPAI between patients who did and did not undergo VSD closure. Statistical calculations were performed with the use of SPSS for Windows version 6.01 (SPSS Inc., Chicago, Ill.). All p values of less than or equal to 0.05 were considered significant. Physiologic data are tabulated.

Results

Demographic data and the morphologic features of the MAPCAs and true pulmonary arteries are summarized in Tables I and II.

Early outcome. Two early deaths occurred in group I, one related to acute pulmonary hemorrhage and one related to postbypass multiple organ failure of unclear origin. Both deaths occurred despite good hemodynamics. In one other patient, who also had postbypass end-organ injury, the VSD was reopened after the operation because of hemodynamic instability (Fig. 2). Although the immediate postbypass right ventricular pressures were high but subsystemic, right ventricular pressures later increased further with consequent compromise in systemic output.

In group II (Fig. 2), one patient continued to be tachypneic after extubation. Cardiac catheterization 10 days after unifocalization revealed a pulmonary/systemic blood flow ratio of 2.4:1. This patient made an uneventful recovery after VSD closure. Another group II patient had multiorgan injuries in the postoperative period and had increased pulmonary blood flow. Because of her fragile and critical status she underwent banding of the right ventricle–pulmonary artery conduit. Subsequently she made a full recovery. Therefore a total of three patients (11%) had significant acute morbidity as the result of an incorrect decision regarding the management of the VSD.

Morphologic data. The pulmonary arterial and MAPCA indices and the TNPAI are summarized in Table III. The TNPAI in patients who underwent VSD closure (median 198 mm^2/m^2; range 79 to 422 mm^2/m^2) was significantly higher ($p = 0.001$; Mann-Whitney U value = 12.0) than in patients in whom the VSD was left open (median 77 mm^2/m^2; range 45 to 173 mm^2/m^2). In addition, a significant correlation ($r = -0.52$ [95% CI, -0.34 to -0.70]; $p = 0.037$) by linear regression existed between the TNPAI and the postoperative pRV/pLV ratio (Fig. 3). However, below 200 mm^2/m^2 a substantial overlap in the TNPAI existed between the patients who did and did not undergo VSD closure (Fig. 2). Among group III patients, one had a TNPAI of 67.5 $mm^2/m^2$and the other had a TNPAI of 101.2 mm^2/m^2. However, both of these patients had long-segment stenosis in four and eight segmental level branches of the collaterals, respectively, and neither had true pulmonary arteries.

Intraoperative pulmonary flow study. The data obtained in six patients are shown in Table IV. In the most recent three patients, the decision was made prospectively to close the VSD on the basis of

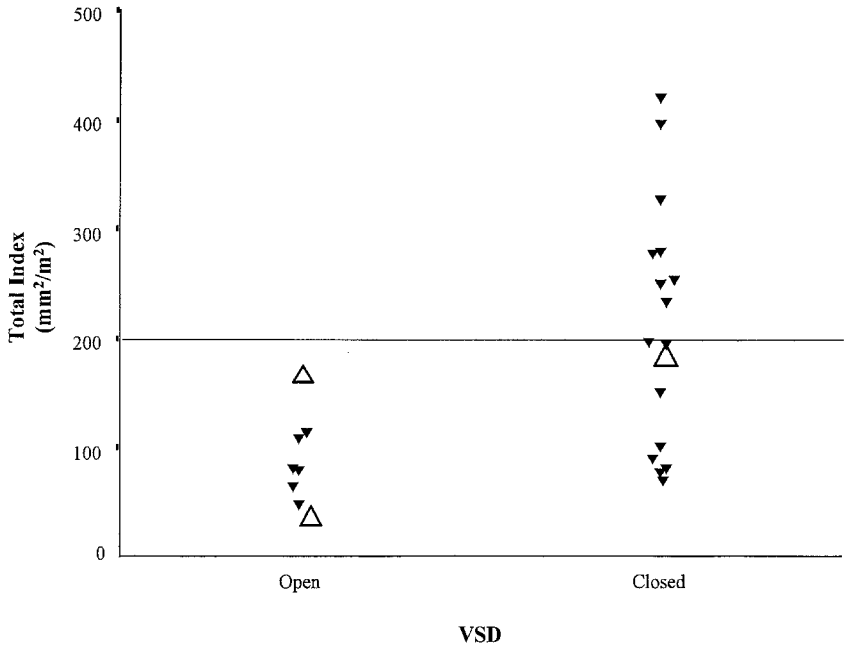

Fig. 2. Distribution of the TNPAI in patients with and without VSD closure. The *upright hollow triangles* represent the patients who required reintervention as a result of an incorrect decision regarding VSD management at the initial operation. The *horizontal line* indicates the separation of patients. Patients with a TNPAI greater than 200 mm^2/m^2 all had the VSD closed uneventfully at the time of unifocalization. Note the significant overlap in VSD status among the patients who are represented below the 200 mm^2/m^2 line. The difference in mean TNPAI was statistically significant ($p = 0.001$).

Table III. *MAPCA, PA, and TNPA indices in patients with the VSD closed and left open*

	BSA (m^2)	*MAPCA index* (mm^2/m^2)	*PA index* (mm^2/m^2)	*TNPA index* (mm^2/m^2)
VSD closed (group I)				
Median	0.23	117	53	198
Range	(0.13-0.38)	(23-422)	(0-294)	(79-422)
VSD open (group II)				
Median	0.30	43	17	77
Range	(0.24-0.38)	(11-173)	(0-138)	(45-173)
p Value	NS	0.053	0.117	0.001

BSA, Body surface area; *MAPCA,* major aortopulmonary collateral artery; *NS,* not significant; *PA,* pulmonary artery; *TNPA,* total neopulmonary artery; *VSD,* ventricular septal defect.

the flow study. The mean pulmonary arterial pressure obtained during the flow study closely approximated the postbypass mean pulmonary arterial pressure (Table IV). The right ventricular systolic pressure was 75% of systemic or less in all of these patients.

Experimental pulmonary flow study. The results of the experimental flow study in lambs are presented in Table V and Fig. 4. As flow increased, so did pulmonary arterial pressure. Postbypass pulmonary arterial pressures were slightly higher than intraoperative pulmonary arterial pressures, which is consistent with bypass-related change in pulmonary vascular resistance, but the differences were not significant.

Discussion

Rationale for the study. In patients having pulmonary atresia with VSD and MAPCAs, our approach is to completely unifocalize the pulmonary

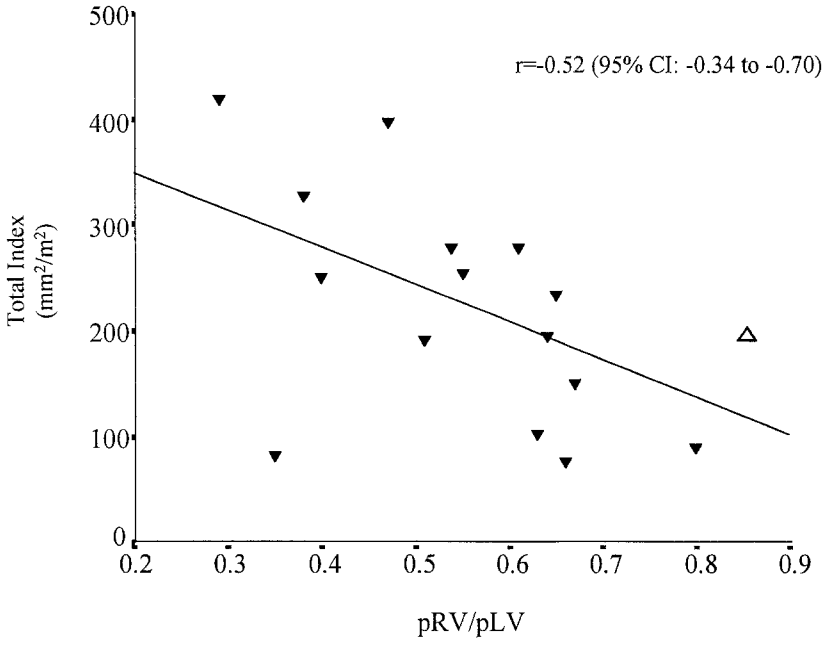

Fig. 3. A significant correlation exists between the TNPAI and postrepair pRV/pLV ratio in patients who underwent one-stage complete repair ($p = 0.037$). The *upright hollow triangle* represents the patient who required early reopening of the VSD as a result of an incorrect decision to close the VSD at the initial operation.

Table IV. *Results of the intraoperative pump flow study*

		During Study			After bypass				
Patient No.	*Assumed cardiac index (L/min/m²)*	*Indexed peak flow (L/min/m²)*	*Mean PAP (mm Hg)*	*Calculated PVR (mm Hg/L/min/m²)*	*Mean PAP (mm Hg)*	*Calculated Qp:Qs*	*Estimated PVR (mm Hg/L/min/m²)*	*VSD status*	*TNPA index (mm²/m²)*
1	2.5	2.94	27	9.2	—	2.5:1	12.5	Open	66
2*	2.5	2.93	36	12.3	—	1.2:1	16.0	Open	*
3	2.5	2.93	40	13.7	36	1:1	11.2	Previously closed	79
4*	2.5	3.11	21	6.8	20	1:1	6.0	Closed	*
5	2.5	2.76	21	7.6	19	1:1	5.6	Closed	83
6	2.5	2.90	27	9.3	26	1:1	6.4	Closed	117

PAP, Pulmonary artery pressure; *PVR,* pulmonary vascular resistance; *Qp:Qs,* pulmonary/systemic blood flow ratio; *TNPA,* Total neopulmonary artery; *VSD,* ventricular septal defect. [Note: See addendum for results in nine additional infants who have undergone complete single-stage repair since this manuscript was submitted.]

*Not infants.

blood flow in one stage through a midline sternotomy, preferably early in infancy.[10] In the majority of patients, we also perform one-stage complete repair, which includes VSD closure and placement of a right ventricle–pulmonary artery conduit in addition to unifocalization. The rationale for our approach is our belief that, left untreated, morphologic changes occur in MAPCAs as a result of flow- and pressure-related damage and that these changes may result in loss of lung segments. Removing the hemodynamic stresses to which the lung segments are subjected early after birth can preserve the lung microvasculature and offers the hope of a good long-term functional result. This approach necessitates the ability to predict successful closure of the VSD with resulting acceptable right ventricular pressure. Because adequate objective criteria for closing the VSD have been lacking, the decision whether to close the VSD at the time of unifocalization has been based on a combination of a subjective assess-

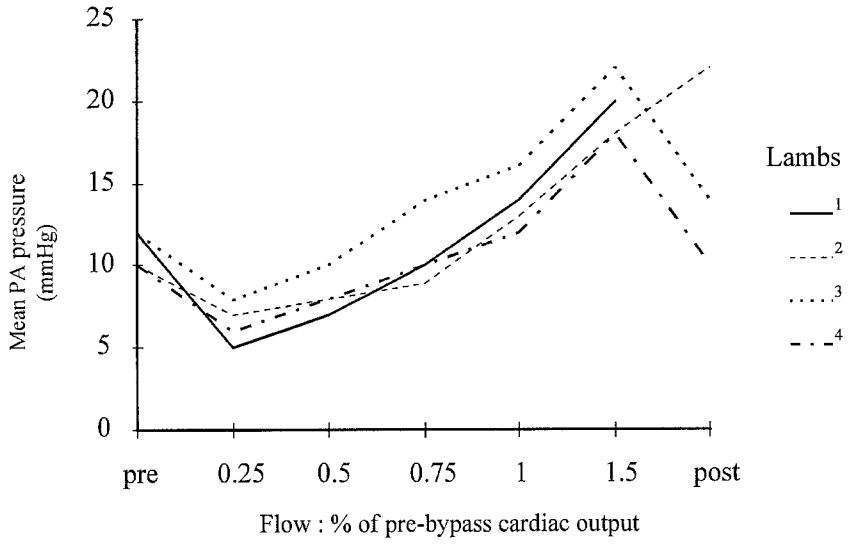

Fig. 4. Relationship of the mean pulmonary artery *(PA)* pressure and the pulmonary blood flow in the normal lambs before the study, during the flow study, and after cardiopulmonary bypass.

Table V. *Results of experimental flow study**

	Qp (ml/min/kg)	*PAP (mm Hg)*	*PVR (mm Hg/ml/min/kg)*
Before bypass	78.6 ± 20.6	11.0 ± 1.2	0.15 ± 0.04
During study	78.6 ± 20.6	13.8 ± 1.7	0.19 ± 0.05
After bypass	92 ± 36.0	15.3 ± 6.1	0.17 ± 0.02

*All values are mean ± standard deviation. *PAP,* Pulmonary artery pressure; *Qp,* pulmonary blood flow (cardiac output); *PVR,* pulmonary vascular resistance.

ment of the collateral supply and an equally subjective assessment of the adequacy of the multiple MAPCA and pulmonary artery anastomoses that were performed.

These subjective decisions have not always been correct. When an incorrect decision is made, a second operation or second bypass run is required either to close or reopen the VSD, and significant multiorgan damage may occur before or as a result of that operation. It is critical that the management of the VSD in these patients be optimized to avoid reoperations and the morbidity related to the incorrect decision. Puga and associates[5] suggested that the VSD be closed if the central pulmonary artery area is greater than 50% of normal, if there is unrestricted peripheral arborization to pulmonary artery segments equivalent to one lung, and if there is evidence of low arterial resistance. Iyer and Mee[7] recommended that the VSD be closed when the predicted pRV/pLV ratio is less than 0.7 according to Kirklin's formula[11] (using pulmonary arterial diameters at the hilum after staged unifocalization), provided no MAPCAs remain, when more than two thirds of lung segments are centralized, and when there is a net left-to-right shunt. Other criteria have also been used.[4] Although these criteria may be valuable in patients who are managed with staged repair, they are not applicable in patients who undergo complete one-stage unifocalization. In our infant patient population, all lung segments are almost invariably unifocalized, and decisions whether to close the VSD must be made during the operation, which eliminates the possibility of deciding this issue on the basis of postoperative evaluation.

Findings of the study. It appears that our subjective assessment regarding VSD closure has generally been correct, but an important group of patients remains (about 10% to 15%) in whom significant morbidity can be attributed to making the wrong decision. Therefore we retrospectively reviewed the angiograms of patients in our series and calculated the cross-sectional area for the entire unifocalized pulmonary vascular supply (MAPCAs and true pulmonary arteries). We found that the TNPAI correlates with the postrepair pRV/pLV ($r = 0.52$; [95% CI, -0.34 to -0.70]; $p = 0.037$; Fig. 3). This observation tells us that the TNPAI is a useful predictor of postrepair pRV/pLV ratio. However, below 200

mm^2/m^2 a considerable overlap in the TNPAI exists between patients with an open or a closed VSD (Fig. 2). To make a decision prospectively on the basis of the TNPAI alone may also be invalid in this overlap group, most importantly because there are many potential points during the subsequent reconstruction for technically imperfect unifocalization, which may affect total pulmonary vascular resistance. Nevertheless, this index is of some benefit, inasmuch as it clearly shows that the VSD can always be closed in patients with a TNPAI of greater than 200 mm^2/m^2.

In patients with a TNPAI of less than 200 mm^2/m^2, physiologic data obtained from the pulmonary flow study combined with the morphologic index may be of significant value. The intraoperative pump flow study, performed during bypass before rewarming the patient, provides the advantage of allowing a decision to be made at the time of complete unifocalization. Most important, it reflects the level of technical precision achieved during the unifocalization. This obviates reoperation or reinstitution of bypass to close or open the VSD. Because the pulmonary flow is nonpulsatile, only a mean pulmonary arterial pressure is measured and total pulmonary vascular resistance can be calculated. Mean postbypass pulmonary arterial pressures have compared favorably with the data obtained during the flow study, although we do not yet have any data on late pulmonary arterial pressures in these patients. In the first two patients in whom the flow study was performed, the data were not used to make a decision regarding VSD closure. In both patients the VSD was left open. The pulmonary/systemic blood flow ratios determined after bypass suggest that the intraoperative flow study data are of predictive value. In the first patient, a lower mean pulmonary arterial pressure was obtained and postbypass pulmonary flow was high. In the second patient, the flow study pulmonary arterial pressure was substantially higher, and postbypass pulmonary blood flow was limited. In the third patient (in whom the VSD was previously closed), the flow study pulmonary arterial pressure correlated closely with postoperative mean pulmonary arterial pressure. In the last three patients, the low mean pressures during the flow study were used as a basis for deciding to close the VSD. Postoperative mean pulmonary arterial pressures correlated closely with pressures obtained during the flow study in all cases, despite low TNPAIs in these patients. This observation is supported by the data from the study in lambs (Table V). Although it is important to note that these lambs were normal, the purpose of this study was to demonstrate the relationship between flow and pressure under conditions of cardiopulmonary bypass and its correlation with postbypass pulmonary arterial pressure. Although the number of lambs is too small for any statistical analysis, the consistency (precision) of the data lends validity to the intraoperative pulmonary flow study.

Although we believe that the flow studies provide an important addition to methods for determining whether to close the VSD, they have a number of limitations that must be acknowledged. They are performed at hypothermia with hemodilution, they use nonpulsatile (and hence nonphysiologic) flow, and they generally do not allow us to distinguish between the effects of pulmonary artery stenosis and pulmonary vascular obstructive disease.

Conclusions

In summary, morphologic criteria combined with intraoperative physiologic data will minimize the errors in decision-making regarding the timing of VSD closure in patients with pulmonary atresia with VSD and MAPCAs. This will allow us to avoid reoperations to close or reopen the VSD and will also minimize the morbidity related to incorrect decisions. These criteria are expected to optimize the outcome of one-stage unifocalization. Further follow-up of our current cohort of patients, along with prospective application of morphologic and physiologic criteria in future patients, will be necessary before the predictive value of these indices for VSD management can be fully evaluated.

Addendum

Since this study was submitted for publication, we have performed complete one-stage unifocalization in eight additional infants. In all of these patients, the intraoperative pump flow study was performed and used prospectively to decide whether to close the VSD. In seven of these infants, the mean pulmonary arterial pressure obtained at a cardiac index of 2.5 ml/min per square meter during the flow study was less than 24 mm Hg and the VSD was closed on the basis of this information. In the remaining patient, the pulmonary arterial pressure during the flow study was elevated and the VSD was left open. Mean pulmonary arterial pressures after discontinuation of cardiopulmonary bypass and rewarming in all seven of the patients who underwent VSD closure was within 5 mm Hg of the value obtained during the intraoperative study (in six of the patients, pressures were within 2 mm Hg). The median postoperative pRV/pLV in these seven patients was 0.39 and was less than 0.5 in all cases. This additional experience further validates the intraoperative

pump flow study as a method for assessing pulmonary vascular resistance during cardiac operations.

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Discussion

Dr. Hillel Laks *(Los Angeles, Calif.).* In this report Dr. Hanley and his associates described an experience with 27 infants undergoing attempted complete unifocalization and repair, and they have attempted to define criteria for closing the VSD. They have used two methods. The first is a morphologic measurement of the size of the true pulmonary arteries and of the collateral arteries just distal to the site of anastomosis. The TNPAI had a rough correlation with the ability to close the VSD and with the subsequent pRV/pLV ratio. However, because it does not take into account anastomotic stenoses or kinks or distortion in the vessels, this index seems to be an unreliable method for the individual patient. In fact, their experience confirmed this limitation. And with flow measurement, I think that VSDs were closed in three patients in whom the TNPAI was below this critical level.

The second method was to perfuse blood from the pump through the homograft while measuring pressure and resistance. This was done in six patients and used prospectively in three. The data presented from this limited experience seem insufficient to draw conclusions on its reliability. Dr. Hanley, are you concerned that this measurement obtained in the bypass situation without the use of inotropic drugs will correlate with the postbypass state and the postextubation measurements where there are problems, such as pulmonary vasospasm or edema, which would not be seen in the operating room and may not be seen in the experimental models in lambs? Are there dangers from this method? Did you see any problems in your patients, such as disruption of delicate suture lines, edema of portions of the lung, or hemorrhage into the lung?

We believe that there are different categories of patients with MAPCAs—those in whom the true pulmonary arteries are the dominant blood supply and those in whom the dominant blood supply is the true pulmonary artery. In fact, their data showed that the majority of those who underwent complete repair with VSD closure had true pulmonary arteries, with half or more of the size of the pulmonary arteries coming from the true pulmonary arteries.

The data presented in this paper continue to raise concerns regarding the wisdom of attempting one-stage repair, particularly in the group with dominant MAPCAs. The literature is replete with reports of the failure of unifocalizations because of stenoses of previously placed end-to-end or end-to-side anastomoses. One would expect this to be a much greater problem when this procedure is performed in infants and through a midline approach, where exposure of these vessels, often within the parenchyma of the lung to get beyond the stenoses, may not be possible.

The pRV/pLV ratio was below 50% in only five of the 16 patients undergoing complete repair, and it was above 60% in eight of the 16 patients. What will happen as these patients grow? Will the anastomoses grow? What will be the pRV/pLV ratio when that happens? Can one rely on stent dilatation of infant-sized anastomoses, and can these be dilated up to adult-sized anastomoses in areas that may be difficult to access? If they cannot be dilated and the pRV/pLV ratio rises as the patients become adolescents and adults, one will be faced with difficult reoperations and possibly the need for lung transplantation.

We continue to pursue a policy of performing early repair only in cases in which the true pulmonary arteries are the dominant source of pulmonary blood supply rather than the MAPCAs. If the MAPCAs are dominant, we intervene in the first 6 months to encourage growth of the true pulmonary arteries if they are present, and, when

necessary, to band collateral vessels that do not have stenoses to protect the patients from pulmonary vascular disease. Staged pericardial unifocalizations, which we have done in more than 60 patients, can be very safely done, with a mortality of only one patient in 60, and subsequent complete repair can also be done with a very low mortality.

Dr. Hanley, could you comment on your intermediate-term results with regard to this issue of restenosis and the pRV/pLV ratio in those patients with dominant MAPCAS who have been followed up for several years? Among the 27 patients, 16 had complete repairs; four, although unifocalized, had their source of blood flow from a shunt, and two had staged procedures. Could you comment on which subgroup of patients you would see as needing a staged procedure rather than undergoing the attempted complete repair with all of its difficulties in terms of assessing whether the VSD should be closed? Could you also comment on how these patients do, the length of hospital stay, and their difficulties in the postoperative course? We have used an adjustable VSD in two patients who had borderline pulmonary artery pressures and resistances. We used a snare that could adjust the VSD from the outside, which we were able to both open and close as necessary in the postoperative course. Have you considered using an adjustable VSD?

You are to be congratulated for taking a bold approach to this challenging problem. The intermediate and particularly the long-term results will define whether this is an extensive and high-risk form of palliation or the definitive means to a biventricular repair, particularly in those groups with dominant MAPCAs.

Dr. Bruce A. Reitz *(Stanford, Calif.).* Dr. Hanley, I have two quick points that I would like you to address on the basis of your experience. First, although you did not present the older age group, at what age does pulmonary vascular resistance become a problem in these large, unobstructed MAPCAs? Second, do the patients in whom the MAPCAs provide the predominant blood supply respond to nitric oxide in a manner similar to those whose blood supply is predominantly via the pulmonary arteries?

Dr. Hanley. I would like to thank both Dr. Laks and Dr. Reitz for their comments. I will try to address most of the questions.

I completely agree with Dr. Laks' first point that more data are needed. I see the present analysis not as a definitive study but as an ongoing examination of these patients. With these patients, we are required to make decisions that often have a moral component to them. If one examines the literature on patients who are born with this lesion, about half of them die within several months to a year of birth. A staged approach to correction results in an ongoing selection process that identifies the best possible candidates who will ultimately undergo complete repair. This unfortunately is only a small percentage of all patients born with this lesion. This has been the stimulus to move ahead with a more aggressive approach in the younger infants. I present these data with a definite degree of caution. However, our experience encourages us to continue to use this approach. The mortality numbers that we have shown and the early results that we have obtained from the flow study are encouraging. The collateral size index numbers are also very helpful for those patients who have indices above a certain level, because we seem to have made the correct decision in essentially all of those.

I believe there are potential dangers to the flow study. These hearts are not beating, and when a full cardiac output is pumped through the pulmonary artery, the left atrium gets full of blood very quickly. It is important to vent the left atrium extremely aggressively during the study. Caution must be exercised. If we have a patient in whom 0.5 cardiac output results in a mean pulmonary arterial pressure of 40 mm Hg, then we would not continue to increase flow. We would already have our answer. If the pulmonary arterial pressures were to rise significantly higher, we would likely see pulmonary hemorrhage. In practice, we have not seen any more pulmonary hemorrhage in the six patients who have been studied than in our previous group of 35 patients. Many patients undergoing unifocalization have some blood-tinged bronchial secretions when they are weaned from the pump and for the first 24 to 8 hours after the operation.

You mentioned the distinction between dominant MAPCAs and dominant true pulmonary arteries. The great majority of these 27 infants had dominant MAPCAs with, on average, only five segments of lung out of the 20 potential segments being fed by true pulmonary arteries and, on average, 15 of the segments supplied by MAPCAs alone. Of the 27 patients, 10, or 38%, had no intrapericardial pulmonary arteries, which is four to five times the percentage found in pathologic series. Twelve of the other patients had stringlike (1 mm diameter or less) true confluent central pulmonary arteries. Thus 22 of the 27 had extraordinarily small or absent pulmonary arteries with the majority of the blood being supplied to the lungs by MAPCAs. We do not make a distinction between patients in whom the MAPCAs are dominant and those in whom the true pulmonary arteries are dominant.

The potential for the development of stenoses after unifocalization is a major concern. We, however, believe that these collaterals are in a sense innocent bystanders. The reason they become stenotic is that after birth the pressure differential is great between the aorta and the distal pulmonary vasculature. The high velocity of flow results in shear forces that cause intimal thickening, vessel elongation, and ultimately kinking and stenoses. It is very interesting that stenoses are not found in patients who are catheterized during the first several days after birth, and they are not found in fetal specimens. They do, however, occur extraordinarily rapidly in the first few weeks and months after birth. We have had experience with several patients who were catheterized in the first few days after birth and had large collaterals and good systemic saturations. When desaturation developed, sometimes as early as 4, 5, or 6 weeks later, they were again catheterized and major stenoses had already developed. If stenoses do not develop during 40 weeks of gestation, but then do develop aggressively within weeks of birth, I believe that there is a hemodynamic phenomenon responsible rather than an intrinsic problem in the collateral vessels. Our philosophy is that if the collateral arteries can be removed from the abnormal hemodynamic environment and placed into a laminar flow situation with lower pressures and controlled

flow, the collaterals will behave better. We have had some patients who have come back after complete unifocalization for balloon dilation and stenting of the vessels; however, the stenoses have almost always been at anastomotic sites. We continue to learn how to perform the anastomoses better, and we have had fewer of these stenoses recently. Interestingly, we have not yet seen a neostenosis remote from an anastomosis in a collateral vessel, which supports the contention that these vessels are innocent bystanders.

The question of the pLV/pRV ratio is a very important one. We all rely on the pLV/pRV ratio for clinical decision-making; however, if we look back at the origin of that ratio from Dr. Kirklin's work, it was measured in patients who were often 2, 3, and 4 years old at the time of complete repair for tetralogy of Fallot. In such patients the mean systemic pressure might be 70 or 80 mm Hg, that is, more similar to mean pressures of adults. A sedated, paralyzed 2-month-old infant weighing 4 kg, however, may have a systemic mean pressure of 38 to 40 mm Hg. In the early postoperative period, these low values tend to give rise to high pRV/pLV ratios, even though absolute right ventricular pressures are quite low. The majority of our patients had absolute right ventricular peak pressures lower than 40 mm Hg, and a few had pressures between 40 and 50 mm Hg. Using the classic pRV/pLV ratio as a predictor of long-term outcome may not be appropriate in infants. To my knowledge, it has never been shown to be appropriate as a long-term predictor of outcome after surgery for tetralogy of Fallot of any kind in infants, whether it be simple tetralogy or with MAPCAs. Regarding intermediate results, we have had some intermediate mortality in both the older patient group and the infant patient group, but the great majority of patients who underwent complete unifocalization have done well. We are analyzing now the risk factors for late mortality, and the early suggestions from the analysis are that the patients who have syndromes, for example, DiGeorge's syndrome, are the patients who have had late, unexplained deaths within the first year of life. One of our patients died of sudden hemoptysis.

Each patient in whom a systemic–pulmonary artery shunt was placed was unique. For example, one of the patients came to us after having had mechanical ventilation for a month in an intensive care unit with an oxymetazoline HCl (Neo-Synephrine) drip. I was reluctant to crossclamp the heart under those conditions. I might emphasize that the highest priority is to do a complete tissue-to-tissue unifocalization to get all of the MAPCAs connected, thereby preserving growth potential and normalizing hemodynamics. The right ventricle–pulmonary artery conduit and VSD closure are not critical to the first operation; however, we perform these procedures as often as possible. We have had three or four extremely sick patients in whom we have been hesitant to incise the right ventricle; we have thus performed the complete unifocalization with a shunt, thereby avoiding the aortic crossclamp and injury to the right ventricle.

We have not used an adjustable VSD; however, if our flow study predictions do not work out, we may well try using a one-way flap valve VSD or an adjustable VSD. In some patients this is certainly an option. It is much better than having to reinstitute bypass to open the VSD.

To respond to Dr. Reitz, in this lesion pulmonary vascular obstructive disease develops rapidly, as fast as it does in any other arterial level shunt, such as truncus or a large ductus arteriosus. For example, I would begin to get concerned within 3 to 6 months if a collateral vessel was not stenotic. We have used nitric oxide in only one or two of the patients. However, what we have found is that right ventricular pressures that have made us a little uncomfortable have resulted from proximal "conduit" type limitations rather than distal pulmonary microvasculature problems. When we have catheterized those patients, the pressures very far out in the pulmonary arteries were usually quite low. Not surprisingly, nitric oxide has not been helpful. If our patient population were older, with more potential for pulmonary vascular obstructive disease, we might have a different experience.